REMARKS

Claims 1 - 4 and 7 - 10 are pending in this application. Claims 1 - 3 and 7 - 9 stand withdrawn as being directed to a non-elected invention.

Claim 4 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Kirchengast et al. in view of Srivatsa et al. on the grounds that it would have been obvious to combine the endothelin blockers taught by Kirchengast et al. with the selective $\alpha_v\beta_3$ integrin antagonist taught by Srivatsa et al. The Office Action further states that "It would have been *prima facie* obvious, within the meaning of 35 U.S.C. 103 to employ these components in combination for their known functions and to optimize the amount of each additive".

The Office Action has not established a *prima facie* case of obviousness. In order to have a *prima facie* case of obviousness, there must be a specific suggestion or motivation to modify the reference, there must be an expectation of success and the prior art reference must teach or suggest all of the claim limitations.

The Office Action has not pointed to any suggestion or motivation for one skilled in the art to modify Kirchengast et al., nor has the Examiner presented any line of argument as to why one skilled in the art would be motivated to combine an ETA endothelin blocker and an $\alpha_v\beta_3$ integrin receptor antagonist. As stated in *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985):

> To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to

> have been obvious in light of the teachings of the references. (emphasis added)

Without such an express suggestion or an explanation as to why the Office Action alleges the claims to be obvious, the standard for a *prima facie* case of obviousness is not met.

Neither Kirchengast et al. nor Srivatsa et al. teach or suggest all the claim limitations. Kirchengast et al. is directed to the use of ET receptor antagonists in restinosis. Nowhere does Kirchengast et al. teach or suggest combining ET_A endothelin blocker and an $\alpha_v\beta_3$ integrin receptor antagonist. Srivatsa et al. is directed to $\alpha_v\beta_3$ integrin blockade limiting neointimal hyperplasi and lumen stenosis following deep coronary arterial stent injury.

When the prior art fails to suggest the claimed invention, as it does here, any reconstruction of the prior art to obtain that invention necessarily and inevitably requires impermissible hindsight. As explained by the CAFC in W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F. 2d 1540, 1553 (Fed. Cir. 1983), 220 USPQ 303, 312-13, cert. denied 53 U.S.L. Week 3239 (October 1, 1983):

> To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.
>
> It is difficult but necessary that the decision-maker forget what he or she has been taught at trial about the claimed invention and cast the mind back to the time the invention was made (often as here many years), to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art.

Other citations:

"When prior art references require selective combination by the court to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself". ACS Hospital Systems, Inc. v. Montefoire Hospital, 732 F. 2d 1572, 1577 & n. 14, 221 USPQ 929, 933 & n. 14 (Fed. Cir. 1984). "There must be 'something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination". Lindemann Maschinefabric GmbH v. American Hoist and Derrick Co., 730 F. 2d 1452, 1462, 221 USPQ 481, 488 (Fed. Cir. 1984), Interconnect Planning Corp. v. Feil, 774 F. 2d1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985).

Applicants submit that the Office Action relies upon the teachings of the instant application rather than what is actually motivated by the prior art. This is a telltale sign that hindsight has been used to formulate the obviousness rejection. Another sign is that the cited prior art references, even if taken together, do not result in the invention of claim 4.

In order for an invention to be considered obvious under 35 U.S.C. 103(a), the invention must be considered as a whole, there must be some motivation or suggestion in the prior art reference itself to modify the reference, and there must be a reasonable expectation of success.

The Court of Appeals for the Federal Circuit has stated the following on the issue of obviousness:

> Uniroyal, Inc. v. Rudkin-Wiley Corp., 837 F. 2d 1044, 1051-52, 5 USPQ 1434, 1438 (Fed. Cir. 1988), cert. denied, 109 S. Ct. 75 (1988), on remand, 13 USPQ2d 1192 (D. Conn. 1989) "Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination."; In re Stencel, 828 F. 2d 751,755, 4 USPQ2d 1071, 1073

> (Fed. Cir. 1987) obviousness cannot be established "by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion that the combination be made.'" Alco*Standard Corp. v. Tennessee Valley Authority*, 808 F. 2d 1490, 1498, 1 USPQ2d 1337, 1343 (Fed. Cir. 1986), cert. dismissed, 108 S. Ct. 26 (1987) "the question is not simply whether the prior art 'teaches' the particular element of the invention, but whether it would 'suggest the desirability, and thus the obviousness, of making the combination.'"; Carella v. Starlight Archery, 804 F. 2d 135,231 USPQ 644 (Fed. Cir. 1986); ACS Hospital Sys., Inc. v. Montefiore Hospital, 732 F. 2d 1572, 221 USPQ 929 (Fed. Cir. 1984) "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so."

Donald S. Chisum, Patents, A Treatise on the Law of Patentability, Validity and Infringement, Vol. 2, 5-218, 1992.

The Office Action also relies upon U.S. 2006/0089374 to support the premise that "combination therapy, **in general**, supports appropriate level dosing in that it allows the application of doses of individual agents lower than those that elicit the unwanted side effects that may occur at higher dose levels." and that "in the case of combining agents that work toward a broadly defined common benefit but which operate through different mechanisms of action, synergistic therapeutic effects may occur".

It should be noted that while this published patent application is being relied upon to show the state of the art at the time the present invention was made, it was filed more than three years after the present application. Surely, that does not reflect state of the art at the time the present invention was made.

For the above noted reasons, it is submitted that claim 4 is patentable under 35 U.S.C. §103(a) and its rejection should be withdrawn.

Claim 10 has also been rejected under 35 U.S.C. §103(a) as being unpatentable over Kirchengast et al. in view of Srivatsa et al. and U.S. Patent 4,761,406. This rejection in respectfully traversed for the reasons set forth above.

Reconsideration and allowance of claims 4 and 10 is respectfully requested.

Respectfully submitted,

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